protein-nucleic acid complexes in and out of the nucleus is an essential step in many host-pathogen interactions such as viral and bacterial infection. Nuclear traffic occurs exclusively through the nuclear pore complex (NPC). While small molecules (up to 40-60 kDa) diffuse through the NPC, nuclear import of larger molecules is mediated by specific Nuclear Localization Signal (NLS) sequences contained in the transported molecule (Garcia-Bustos et al. 1991; Dingwall 1991). Most NLSs can be classified in three general groups: (i) a monopartite NLS exemplified by the SV40 large T antigen NLS (SEQ ID NO:3: PKKKRKV); (ii) a bipartite motif consisting of two basic domains separated by a variable number of spacer amino acids and exemplified by the Xenopus nucleoplasmin NLS (SEQ ID NO:4: KRXXXXXXXXXXXKKKL); and (iii) noncanonical sequences such as M9 of the hnRNP A1 protein, the influenza virus nucleoprotein NLS, and the yeast Gal4 protein NLS (Dingwall and Laskey 1991).

After the Abstract:

Delete the previously filed SEQUENCE LISTING pages 1-6.

Add new SEQUENCE LISTING pages 1-6, enclosed herewith.

REMARKS

In accordance with the sequence rules, applicants have enclosed the following:

1. A computer readable form (CRF) copy of the new Sequence Listing in the form of a 3 1/2" diskette;
2. A paper copy of the new Sequence Listing, pages 1-6; and
3. A statement that the content of the paper and computer readable form are the same and include no new matter.

The Sequence Listing has been corrected to indicate the amino acids represented by Xaa in SEQ ID NO:4. An additional Xaa

residue has been added to SEQ ID NO:4. Support for the addition of an Xaa residue, and for the particular amino acids represented by Xaa in SEQ ID NO:4, can be found in the reference cited for the teaching of the *Xenopus* NLS (Dingwall and Laskey 1991). Since the sequences as presented in the replacement Sequence Listing were presented in the specification as originally filed or in the literature reference that was incorporated by reference, no new matter is involved. Applicants respectfully request that the Sequence Listing be entered and maintain that the application now complies with the sequence rules.

Please direct any questions regarding this communication to applicants' undersigned attorney.

Respectfully submitted,

Dated: March 26, 2001

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date below.

03/26/01
Date

Susan J. Braman
Attorney Reg. No.: 34,103

U.S. Serial No. 09/435,274

Marked-Up Version of Paragraph(s):

Nucleo-cytoplasmic shuttling of protein molecules is a basic biological process central to the regulation of gene expression (which underlies all aspects of development, morphogenesis, and signaling pathways in eukaryotic organisms). Furthermore, transport of proteins and protein-nucleic acid complexes in and out of the nucleus is an essential step in many host-pathogen interactions such as viral and bacterial infection. Nuclear traffic occurs exclusively through the nuclear pore complex (NPC). While small molecules (up to 40-60 kDa) diffuse through the NPC, nuclear import of larger molecules is mediated by specific Nuclear Localization Signal (NLS) sequences contained in the transported molecule (Garcia-Bustos et al. 1991; Dingwall 1991). Most NLSs can be classified in three general groups: (i) a monopartite NLS exemplified by the SV40 large T antigen NLS (SEQ ID NO:3: PKKKRKV); (ii) a bipartite motif consisting of two basic domains separated by a variable number of spacer amino acids and exemplified by the Xenopus nucleoplasmin NLS (SEQ ID NO:4: KRXXXXXXXXXXXKKKL); and (iii) noncanonical sequences such as M9 of the hnRNP A1 protein, the influenza virus nucleoprotein NLS, and the yeast Gal4 protein NLS (Dingwall and Laskey 1991).